REMARKS

As an initial matter, Applicants respectfully request entry of the amendments set forth in the response filed on October 17, 2003. Claims 1-81 (as shown above) reflect the claims after such entry.

New claim 82 has been added. The new claim is substantially the same as pending claim 50, except that language relating to the standard EPC isolation assay has been removed. New claim 83 includes that language.

The new claims 82-83 find support throughout the instant application including the claims as filed originally. No new matter has been added by virtue of the new claims.

As a further matter, Applicants submit herewith a signed Declaration under 37 CFR 1.131. The Declaration is the same as the one previously submited except the instant Declaration has the signature of inventor Asahara. Consideration of the signed Declaration is requested.

Applicants respond to comments made on the Advisory Action dated December 9, 2003 as follows.

In part 2 of the Advisory Action, the position was taken that Applicants' amendment of claim 50 to include a rodent or primate mammal would raise new issues requiring consideration particularly under 35 USC §112, first paragraph. Applicants respectfully disagree with this position.

Applicants' disclosure fully satisfies the "how to make" and "how to use" requirements of 35 USC §112, first paragraph. Specific support for the amendment can be found at pgs. 7-8, bridging paragraph for instance (disclosing particular mammals for use with the invention such as rodents and primates). As disclosed at pg. 8, lines 1-8, for instance, manipulation of such

mammals in accord with the invention is useful, for instance, because the animals represent accepted models of human disease. Practice of the invention in such preferred models is fully enabled by the instant specification and is particularly useful eg., as a way of fine-tuning treatment of certain primates such as human patients.

In part 5 of the Advisory Action, the Office maintained the obviousness rejection in view of the Hammond patent on grounds that: 1) the Declaration of Dr. Asahara was unsigned; and 2) the Declaration was not commensurate with the scope of the proposed claims.

Applicants have addressed the first basis of maintaining the rejection by submitting herewith the signed Declaration of Dr. Asahara. As to the second basis, Applicants must respectfully disagree with the USTPO.

The Office asserts that the obviousness rejection will be maintained because the Declaration is not commensurate with the scope of the proposed claims. Respectfully, that is not a correct standard for reviewing a Declaration under Rule 131. To the extent the attached signed Declaration will be reviewed under this standard, the obviousness rejection cannot withstand scrutiny and should be withdrawn.

The USPTO and the Federal courts have long held that a Rule 131 Declaration is sufficient for antedating a reference if it can establish possession of subject matter falling within the claimed invention such that the claim at issue reads on it. Applicants are not aware of any rule or case law that requires them to submit a Declaration commensurate with the scope of the proposed claims to antedate the Hammond patent. Indeed, MPEP 715.02 states that:

> The 37 CFR 1.131 affidavit or declaration must establish possession of either the whole invention or something falling within the claim (such as a species of a claimed genus), in the sense that the claim as a whole reads on it (citing *In re Tanczyn*, 347 F.2d 830, 146 USPQ 298 (CCPA 1965).

Applicants' Rule 131 Declaration fully satisfies this standard. For instance, and as

already admitted by the Office, the Declaration "showed that Applicants induced formation of new blood vessels in mice and rabbits using granulocyte-macrophage colony stimulating factor (GM-CSF) prior to 9/19/97)...". Advisory Action at pg. 3. As Dr. Asahara makes clear in the Declaration, subject mammals had ischemia and addition of the GM-CSF was shown to produce new blood vessel growth. Decl. At ¶s 7, 9-13, for instance. In particular, chronic isechemia was treated by GM-CSF resulting is new blood vessel growth. Decl. at ¶ 13. Thus, the invention embodiment referred to by the Office clearly falls within the scope of the claimed invention (see amended claim 50 and new claim 82). On this basis alone, the Rule 131 Declaration is sufficient to antedate the Hammond patent and such action is requested.

Applicants urge that the instant Declaration is sufficient on other grounds.

For example, **Exhibits 1 and 2** of the signed state, among other things, that:

> We investigated the hypothesis that EPC kinetics in circulation may have significant role in control of neovascularization, and hematopoieteic mobilization with **cytokines, such as granulocyte macrophage-colony stimulating factor (GM-CSF),** known to enhance hematopoietic progenitors into peripheral blood, may enhance EPC kinetics and contribute to neovascularization in severe ishemia.

> The concept of **cytokine-induction** of EPC mobilization could be a novel and promissing [sic] strathegy [sic] for clinical application to ischemic vascular disease, which lacks efficient blood supply.

Clearly, a worker reading those statements in the context of Applicants's specification and the entire Declaration would appreciate that the inventors possessed the claimed invention well before Hammond's priority date. That is, before Hammond's priority date Applicants learned that one could induce new blood vessels in a mammal (such as a patient) having ischemia by using GM-CSF as well as other suitable cytokines.

As it considers the signed Declaration, the Office is respectfully reminded that Applicants' possession of what is shown to have been reduced to practice prior to

Hammond's date carries with it possession of variations and adaptations which would, at the same time, have been obvious to one skilled in the art. See MPEP 715.02 and *In re Spiller*, 500 F. 2d. 1170, 182 USPQ 614 (CCPA 1974). Put another way, it is improper for the Office to allege that the instant Declaration is improper on grounds that the evidence contained therein it is not commensurate with the scope of the pending claims. A broader reading of the Declaration is required by the MPEP and the case law. Thus at the very least Applicants have shown not only possession of a method for inducing formation of new blood vessels in mice and rabbits using GM-CSF (as acknowledged by the USPTO) but also variations and adaptations of that method that would be understood by workers in this field.

In view thereof, reconsideration and withdrawal of the instant obviousness rejection are requested.

CONCLUSION

Applicants submit that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

Although it is not believed that any fee is needed to consider this submission, the Examiner is authorized to charge our Deposit Account No. **04-1105** should such fee be deemed necessary.

Respectfully submitted,

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